

What is claimed is:

1. A liquid composition for direct pulmonary delivery of a pharmaceutically active agent to a patient in need of treatment comprising:

5 a) a pharmaceutically effective amount of said active agent; and
 b) a liquid carrier vehicle, wherein said liquid carrier vehicle consists essentially of:
 i) from about 30% v/v to about 99% v/v of a liquid fluorocarbon;
 ii) from about 1% v/v to about 70% v/v of a co-solvent;
 iii) from about 0% w/v to about 10% w/v of a phospholipid; and
10 iv) from about 0% w/v to about 10% w/v of a pharmaceutically acceptable excipient;

wherein said active agent is dissolved or suspended in said liquid carrier vehicle and wherein said liquid composition has a surface tension of from about 15 dyne/cm to about 40 dyne/cm.

15 2. The composition according to claim 1 wherein said fluorocarbon is present in said carrier vehicle at from about 50% v/v to about 95% v/v.

 3. The composition according to claim 2 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

20 4. The composition according to claim 1 wherein said fluorocarbon is selected from the group consisting of 1,1,1,3,3-pentafluorobutane, 1,1,1,3,3-pentachlorobutane, 1,1-dichloro-1,3-difluorobut-2-ene, 1-chloro-1,1,3-trifluorobut-2-ene, perfluorobutylethane, hexafluoroisobutylene, hexafluoroisopropane, perfluoromethane, perfluoroethane, perfluoropropene, perfluorobutane, perfluorocyclobutane, perfluoropentane, perfluorohexane, perfluoroctane, perfluoroctyl bromide, perfluoroctyl iodide, perfluorodecalin and
25 perfluoronaphthalene.

 5. The composition according to claim 4 wherein said fluorocarbon is selected from the group consisting of perfluoroctyl bromide and perfluorodecalin.

 6. The composition according to claim 5 wherein said fluorocarbon is present in the carrier vehicle at from about 50% v/v to about 95% v/v.

30 7. The composition according to claim 6 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

 8. The composition according to claim 1 wherein said co-solvent is selected from the group consisting of alcohols, ethers and alkyl sulfoxides.

 9. The composition according to claim 8 wherein said co-solvent is ethanol.

10. The composition according to claim 9 wherein said ethanol is present in said carrier vehicle at from about 5% v/v to about 50% v/v.

11. The composition according to claim 10 wherein said ethanol is present in the carrier vehicle at from about 5.0% v/v to about 35% v/v.

5 12. The composition according to claim 3 wherein said ethanol is present in the carrier vehicle at from about 5% v/v to about 35% v/v.

13. The composition according to claim 1 wherein said phospholipid is selected from the group consisting of phosphatidic acid, phosphatidylethanolamine, lecithin, phosphatidylglycerol, diphosphatidylglycerol, dipalmitoylphosphatidylcholine, 1-palmitoyl-2-oleoyl-phosphatidylglycerol, dipalmitoylphosphatidylglycerol, as well as mixtures of such phospholipids

14. The composition according to claim 13 wherein said phospholipid is selected from the group consisting of lecithin, dipalmitoylphosphatidylcholine and 1-palmitoyl-2-oleoyl-phosphatidylglycerol.

15 15. The composition according to claim 13 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 2.0% w/v.

16. The composition according to claim 15 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 1.0 w/v.

20 17. The composition according to claim 1 wherein said pharmaceutically acceptable excipient is selected from the group comprising polyols, antioxidants, anti-microbials, pH adjusting agents, viscosity adjusting agents and salts.

25 18. The composition according to claim 17 wherein said pharmaceutically acceptable excipient is selected from the group consisting essentially of propylene glycol, glycerol, polyvinyl alcohol, polyethylene glycol having an average molecular weight between about 200 and 4000, Vitamin E, Vitamin E TPGS, ascorbic acid, methyl paraben, ethyl paraben, sodium hydroxide, hydrochloric acid, polyvinyl alcohol, polyvinyl pyrrolidone, benzalkonium chloride, sodium chloride and potassium chloride.

19. The composition according to claim 17 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from 0.05% w/v% to about 5.0% w/v.

30 20. The composition according to claim 19 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from about 0.1% w/v% to about 2.5% w/v.

21. A composition according to claim 1 comprising:

- a) a pharmaceutically effective amount of said active agent; and
- b) a liquid carrier vehicle, wherein said liquid carrier vehicle consists essentially of:
 - i) from about 50% v/v to about 95% v/v of a liquid fluorocarbon;
 - ii) from about 5% v/v to about 50% v/v of a co-solvent;
 - iii) from about 0.1% w/v to about 2.0% w/v of a phospholipid; and
 - iv) from about 0.05% w/v to about 5.0% w/v of a pharmaceutically acceptable excipient.

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10 22. A composition according to claim 1 comprising:

- a) a pharmaceutically effective amount of said active agent; and
- b) a liquid carrier vehicle, wherein said liquid carrier vehicle consists essentially of:
 - i) from about 65% v/v to about 95% v/v of a liquid fluorocarbon;
 - ii) from about 5.0% v/v to about 35% v/v of a co-solvent;
 - iii) from about 0.1% w/v to about 1.0% w/v of a phospholipid; and
 - iv) from about 0.1% w/v to about 2.5% w/v of a pharmaceutically acceptable excipient.

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20 23. A liquid carrier vehicle for use with an EHD spraying/aerosolization means consisting essentially of:

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- i) from about 30% v/v to about 99 v/v of a liquid fluorocarbon;
- ii) from about 1% v/v to about 70% v/v of a co-solvent;
- iii) from about 0% w/v to about 10% w/v of a phospholipid; and
- iv) from about 0% w/v to about 10% w/v of a pharmaceutically acceptable excipient.

wherein said liquid carrier vehicle has surface tension of from about 15 dyne/cm to about 40 dyne/cm.

30 24. The liquid carrier vehicle according to claim 23 wherein said fluorocarbon is present in the carrier vehicle at from about 50% v/v to about 95% v/v.

25. The liquid carrier vehicle according to claim 24 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

30 26. The liquid carrier vehicle according to claim 23 wherein said fluorocarbon is selected from the group consisting of 1,1,1,3,3-pentafluorobutane, 1,1,1,3,3-pentachlorobutane, 1,1-

dichloro-1,3-difluorobut-2-ene, 1-chloro-1,1,3-trifluorobut-2-ene, perfluorobutylethane, hexafluoroisobutylene, hexafluoroisopropane, perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, perfluorocyclobutane, perfluoropentane, perfluorohexane, perfluoroctane, perfluoroctyl bromide, perfluoroctyl iodide, perfluorodecalin and

5 perfluoronaphthalene.

27. The liquid carrier vehicle according to claim 26 wherein said fluorocarbon is selected from the group consisting of perfluoroctyl bromide and perfluorodecalin.

28. The liquid carrier vehicle according to claim 27 wherein said fluorocarbon is present in the carrier vehicle at from about 50% v/v to about 95% v/v.

10 29. The liquid carrier vehicle according to claim 28 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

30. The liquid carrier vehicle according to claim 23 wherein said co-solvent is selected from the group consisting of alcohols, ethers and alkyl sulfoxides.

31. The liquid carrier vehicle according to claim 30 wherein said co-solvent is ethanol.

15 32. The liquid carrier vehicle according to claim 31 wherein said ethanol is present in said carrier vehicle at from about 5% v/v to about 50% v/v.

33. The liquid carrier vehicle according to claim 32 wherein said ethanol is present in the carrier vehicle at from about 5% v/v to about 35% v/v.

34. The liquid carrier vehicle according to claim 23 wherein said phospholipid is selected from the group consisting of phosphatidic acid, phosphatidylethanolamine, lecithin, phosphatidylglycerol, diphosphatidylglycerol, dipalmitoylphosphatidylcholine, 1-palmitoyl-2-oleoyl-phosphatidylglycerol, dipalmitoylphosphatidylglycerol, as well as mixtures of such phospholipids.

25 35. The liquid carrier vehicle according to claim 34 wherein said phospholipid is selected from the group consisting of lecithin, dipalmitoylphosphatidylcholine and 1-palmitoyl-2-oleoyl-phosphatidylglycerol.

36. The liquid carrier vehicle according to claim 35 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 2.0% w/v.

30 37. The liquid carrier vehicle according to claim 36 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 1.0 w/v.

38. The liquid carrier vehicle according to claim 23 wherein said liquid carrier vehicle contains a pharmaceutically acceptable salt and wherein said salt is present in said carrier vehicle at from about 0.05% w/v to about 5.0% w/v.

39. The liquid carrier vehicle according to claim 38 wherein said salt is selected from the group consisting of benzalkonium chloride, sodium chloride and potassium chloride or mixtures thereof.

40. The liquid carrier vehicle according to claim 23 wherein said pharmaceutically acceptable excipient is selected from the group comprising polyols, antioxidants, anti-microbials, pH adjusting agents, and viscosity adjusting agents.

41. The liquid carrier vehicle according to claim 40 wherein said pharmaceutically acceptable excipient is selected from the group consisting essentially of propylene glycol, glycerol, polyvinyl alcohol, polyethylene glycol having an average molecular weight between about 200 and 4000, Vitamin E, Vitamin E TPGS, ascorbic acid, methyl paraben, ethyl paraben, sodium hydroxide, hydrochloric acid, polyvinyl alcohol and polyvinyl pyrrolidone.

42. The liquid carrier vehicle according to claim 41 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from 0.05% w/v% to about 5.0% w/v.

43. The liquid carrier vehicle according to claim 42 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from about 0.1% w/v% to about 2.5% w/v.

44. The liquid carrier vehicle according to claim 23 consisting essentially of:

- i) from about 50% v/v to about 95 v/v of a liquid fluorocarbon;
- ii) from about 5% v/v to about 50% v/v of a co-solvent;
- 20 iii) from about 0.1% w/v to about 2.0% w/v of a phospholipid; and
- iv) from about 0.05 % w/v to about 5.0% w/v of a pharmaceutically acceptable excipient.

45. The liquid carrier vehicle according to claim 44 consisting essentially of:

- i) from about 65% v/v to about 95 v/v of a liquid fluorocarbon;
- 25 ii) from about 5.0% v/v to about 35% v/v of a co-solvent;
- iii) from about 0.1 % w/v to about 1.0% w/v of a phospholipid; and
- iv) from about 0.1 % w/v to about 2.5% w/v of a pharmaceutically acceptable excipient.

46. A method for delivering a pharmaceutically active agent to the respiratory tract of a patient in need of treatment comprising the steps of:

- a) preparing a liquid carrier vehicle consisting essentially of:
 - i. from about 30% v/v to about 99 v/v of a liquid fluorocarbon;
 - ii. from about 1% w/v to about 70% w/v of a co-solvent;
 - iii. from about 0.0% w/v to about 10% w/v of a phospholipid;

iv. from about 0.0 % w/v to about 10.0 w/v of a pharmaceutically acceptable excipient;

5 b) dissolving or suspending a pharmaceutically effective amount of said active agent in said liquid carrier vehicle;

c) producing an aerosol of said solution or suspension using an EHD spraying/aerosolization means; and

d) administering said aerosol to the pulmonary tract of said patient via inhalation of said aerosol;

wherein said liquid carrier vehicle has a surface tension of from about 15 dyne/cm to about 40
10 dyne/cm.

47. The method according to claim 46 wherein said fluorocarbon is present in said carrier vehicle at from about 50% v/v to about 95% v/v.

48. The method according to claim 47 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

15 49. The method according to claim 46 wherein said fluorocarbon is selected from the group consisting 1,1,1,3,3-pentafluorobutane, 1,1,1,3,3-pentachlorobutane, 1,1-dichloro-1,3-difluorobut-2-ene, 1-chloro-1,1,3-trifluorobut-2-ene, perfluorobutylethane, hexafluoroisobutylene, hexafluoroisopropano, perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, perfluorocyclobutane, perfluoropentane, perfluorohexane, 20 perfluorooctane, perfluoroctyl bromide, perfluoroctyl iodide, perfluorodecalin and perfluoronaphthalene.

50. The method according to claim 49 wherein said fluorocarbon is selected from the group consisting of perfluoroctyl bromide and perfluorodecalin.

51. The method according to claim 50 wherein said fluorocarbon is present in the carrier
25 vehicle at from about 50% v/v to about 95% v/v.

52. The method according to claim 51 wherein said fluorocarbon is present in said carrier vehicle at from about 65% v/v to about 95% v/v.

53. The method vehicle according to claim 46 wherein said co-solvent is selected from the group consisting of alcohols, ethers and alkyl sulfoxides.

30 54. The method according to claim 53 wherein said co-solvent is ethanol.

55. The method according to claim 54 wherein said ethanol is present in said carrier vehicle at from about 5% v/v to about 50% v/v.

56. The method according to claim 55 wherein said ethanol is present in the carrier vehicle at from about 5% v/v to about 35% v/v.

57. The method according to claim 46 wherein said phospholipid is selected from the group consisting of phosphatidic acid, phosphatidylethanolamine, lecithin, phosphatidylglycerol, diphosphatidylglycerol, dipalmitoylphosphatidylcholine, 1-palmitoyl-2-oleoyl-phosphatidylglycerol, dipalmitoylphosphatidylglycerol, as well as mixtures of such phospholipids.

5 58. The method according to claim 57 wherein said phospholipid is selected from the group consisting of lecithin, dipalmitoylphosphatidylcholine and 1-palmitoyl-2-oleoyl-phosphatidylglycerol.

10 59. The method according to claim 57 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 2.0% w/v.

60. The method according to claim 59 wherein said phospholipid is present in the carrier vehicle at from about 0.1% w/v to about 1.0 w/v.

15 61. The method according to claim 46 wherein said carrier vehicle contains a pharmaceutically acceptable salt and wherein said salt is present in said carrier vehicle at from about 0.05% w/v to about 5.0% w/v.

62. The method according to claim 61 wherein said salt is selected from the group consisting of benzalkonium chloride, sodium chloride and potassium chloride or mixtures thereof.

20 63. The method according to claim 46 wherein said pharmaceutically acceptable excipient is selected from the group comprising polyols, antioxidants, anti-microbials, pH adjusting agents, and viscosity adjusting agents.

25 64. The method according to claim 63 wherein said pharmaceutically acceptable excipient is selected from the group consisting essentially of propylene glycol, glycerol, polyvinyl alcohol, polyethylene glycol having an average molecular weight between about 200 and 4000, Vitamin E, Vitamin E TPGS, ascorbic acid, methyl paraben, ethyl paraben, sodium hydroxide, hydrochloric acid, polyvinyl alcohol and polyvinyl pyrrolidone.

65. The method according to claim 63 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from 0.05% w/v to about 5.0% w/v.

30 66. The method according to claim 65 wherein said pharmaceutically acceptable excipient is present in said carrier vehicle at from about 0.1% w/v to about 2.5% w/v.

67. The method according to claim 46 consisting essentially of:

- i) from about 50% v/v to about 95 v/v of a liquid fluorocarbon;
- ii) from about 5% v/v to about 50% v/v of a co-solvent;

- iii) from about 0.1% w/v to about 2.0% w/v of a phospholipid;
- iv) from about 0.05 % w/v to about 5.0% w/v of a pharmaceutically acceptable excipient.

5. 68. The method according to claim 46 consisting essentially of:

- i) from about 65% v/v to about 95 v/v of a liquid fluorocarbon;
- ii) from about 5.0% v/v to about 35% v/v of a co-solvent;
- iii) from about 0.1% w/v to about 1.0% w/v of a phospholipid;
- iv) from about 0.1 % w/v to about 2.5% w/v of a pharmaceutically acceptable excipient.

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